Helicobacter pylori and proton pump inhibitor therapy: one diagnostic method is enough?

Davide Giuseppe Ribaldone,[a*] Giorgio Maria Saracco,[a] Rinaldo Pellicano[b]

[a] Department of Medical Sciences, Division of Gastroenterology, University of Torino, Corso Bramante 88, 10126, Turin, Italy

[b] Unit of Gastroenterology, Molinette Hospital, Corso Bramante 88, 10126, Turin, Italy

Conflicts of interest: none

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

[*]Corresponding author: Davide Giuseppe Ribaldone - Department of Medical Sciences, Division of Gastroenterology, University of Torino, C.so Bramante 88 - 10126 Torino – Italy. E-mail: davrib_1998@yahoo.com Tel: +390116335208, Fax: +390116336752.

Giorgio Maria Saracco: giorgiomaria.saracco@unito.it

Rinaldo Pellicano: rinaldo_pellican@hotmail.com

keywords: antiplatelet; antithrombotic; bleeding; *Helicobacter pylori*; peptic; proton pump inhibitor

Dear Editor,

In a recent study Negovan et al. assessed the impact of pathological and clinical predisposing factors (histological findings, concomitant drug consumption, comorbidities, symptoms, social habits, *Helicobacter pylori-H. pylori* infection) on severe gastro-duodenal lesions in patients on long-term low-dose aspirin and proton pump inhibitors (PPI) treatment [1]. They enrolled patients with chronic low-dose aspirin and PPI therapy referred for an upper digestive endoscopy between September 2012 and December 2015. Patients attended esophagogastroduodenoscopy for the following reasons: digestive symptoms, anaemia or screening for gastrointestinal bleeding risk (before the initiation of combined antithrombotic therapy, before major surgery). Patients with gastro-duodenal surgery, varices, active severe bleeding or patients in whom a gastric cancer was discovered were excluded. The authors also excluded patients with haematological disorders (leukaemia, lymphoma, aplastic or haemolytic anaemia), as well as patients with severe medical conditions (cancer, cardiac, respiratory, liver or kidney end-stage disease), autoimmune gastritis, dysplasia. Two biopsy specimens from the antrum and two from the corpus were taken for routine histology and were examined by a single pathologist. The observed relative frequency of severe gastro-duodenal lesions was 27.4%. There were no significant differences between cases (modified Lanza score ≥ 3) and controls regarding *H. pylori* status (21/65 cases vs. 52/172 controls, p=0.875). In the univariate logistic regression model, factors associated with severe gastro-duodenal lesions were gender (OR = 1.87, 95% CI: 1.04–3.41), assumption of anticoagulants (OR=2.40, 95% CI: 1.26–4.53), gastric atrophy and/or intestinal metaplasia (OR = 1.85, 95% CI: 1.04–3.32), congestive heart failure (OR = 2.59, 95% CI: 1.16–6.62), anaemia (OR = 3.01, 95% CI: 1.67–5.47) and smoking (OR = 4.29, 95% CI: 1.57–12.32). Anticoagulants (p = 0.04) and anaemia (p = 0.02) were risk factors for severe lesions via multivariate regression analysis.

H. pylori is a slow-growing, micro-aerophilic, Gram-negative bacterium, usually acquired during

childhood, whose natural habitat is the luminal surface of the gastric epithelium. At least 50% of the world's human population carries the microorganism, with a prevalence much higher in developing countries than in developed countries [2]. *H. pylori* infection is accepted as the most important cause of gastritis and peptic ulcer in humans. Both *H. pylori* infection and aspirin/non-steroidal anti-inflammatory drug (NSAID) use are independent risk factors for the development of peptic ulcer and associated bleeding; this risk increases when both factors are present [3]. It is well-known that bacterial cure alone is not sufficient to prevent ulcer bleeding in NSAID users with high gastrointestinal risks, such as a history of ulcer bleeding [4]. Nevertheless, detection and treatment of *H. pylori* remain two key-steps in the strategy for long-term management of these patients.

The methods to diagnose *H. pylori* infection can be classified as invasive or non-invasive, the former being based on biopsy specimens obtained at endoscopy. When a patient needs to underwent upper gastrointestinal endoscopy, due to alarming symptoms or older age *H. pylori* infection should be detected on biopsies taken in the stomach from two topographical locations, the antrum and the corpus.

The authors of the Romanian study [1] searched for *H. pylori* infection performing two biopsies from the antrum and two from the corpus. Thus, this is a correct approach increasing the test's sensitivity in patients currently treated with a PPI drug, but false negative results may still occur if the test is performed within seven days of taking PPIs [5]. Stopping PPIs two weeks before testing would allow the bacteria to repopulate the stomach and the tests previously negative could once again become positive [6]. Regarding the population included by Negovan et al, when possible, PPIs should have been stopped two weeks before the upper gastrointestinal endoscopy. When the suspension of the PPI was considered risky, in patients with a severe gastro-duodenal lesion and *H. pylori* negativity at histology, the evaluation of antibodies to *H. pylori* in serum, though marker of exposure and not necessarily of "true infection", it should have been considered, as a confirmatory test. This could be the best option considering that other non-invasive tests could be falsely negative in patients with bleeding

ulcers or recent use of PPIs.

In conclusion, in this study a second test it should have been done in case of *H. pylori* negativity to confirm this result.

References

[1] Negovan A, Iancu M, Moldovan V, et al. The contribution of clinical and pathological predisposing factors to severe gastro-duodenal lesions in patients with long-term low-dose aspirin and proton pump inhibitor therapy. Eur J Intern Med 2017;44:62-66.

[2] Tonkic A, Tonkic M, Lehours P, et al. Epidemiology and diagnosis of *Helicobacter pylori* infection. Helicobacter 2012;17(Suppl1):1-8.

[3] Huang JQ, Sridhar S, Hunt RH. Role of *Helicobacter pylori* infection and nonsteroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. Lancet 2002;359:14-22.

[4] Malfertheiner P, Chan FKL, McColl KEL. Peptic ulcer disease. Lancet 2009;374:1449-61.

[5] Pellicano R, Ribaldone DG, Fagoonee S, et al. A 2016 panorama of *Helicobacter pylori* infection: key messages for clinicians. Panminerva Med. 2016 Dec;58(4):304-317.

[6] Malfertheiner P, Megraud F, O'Morain CA, et al. Management of *Helicobacter pylori* infection-the Maastricht V/Florence Consensus Report. Gut. 2017 Jan;66(1):6-30. doi: 10.1136/gutjnl-2016-312288. Epub 2016 Oct 5.